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EXAMINER
KERR, KATHLEEN M

ART UNIT	PAPER NUMBER
1652	27

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/449,817	STEINER ET AL.	
	Examiner	Art Unit	
	Kathleen M Kerr	1652	

-- The MAILING DATE of this communication appears on the cov r sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 January 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,7,10-27,30-36,40,44,45,47 and 54-60* is/are pending in the application.

4a) Of the above claim(s) *30-36,40,44,45,47 and 58* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1,7,10-27,54-57,59 and 60* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Application Status

1. In response to the previous Office action, a written restriction requirement (Paper No. 23 mailed September 28, 2001), Applicants filed an election. Claims 1, 7, 10-27, 30-36, 40, 44, 45, 47, and 54-60 are pending in the instant application.

Election

2. Applicant's election with traverse of Group I, Claims 1, 7, 10, 11, 18-27, and 54-60 (elected species = human, SEQ ID NOs:1 and 2) in Paper No. 26 is acknowledged. The traversal is on the ground(s) that Groups II-VIII do not present a search burden on the Examiner to be examined with Group I. This is not found persuasive because searching Groups I-VII would, in fact, present a serious search burden on the Examiner who would be required to search additional class/subclasses that would not be searched for Group I. Thus, since the searches are not co-extensive, a search burden exists.

The requirement is still deemed proper and is therefore made FINAL.

The Examiner will rejoin Group II with the elected Group. Claims 30-36, 40, 44, 45, and 47 are withdrawn from consideration as non-elected inventions. Claims 1, 7, 10-27 and 54-60 are elected as they are drawn to the elected species, human. Since Claim 58 is drawn solely to the rat species (and not the elected human species) (see below), Claim 58 is withdrawn from further consideration as a non-elected invention as well. Thus, Claims 1, 7, 10-27, 54-57, and 59-60 will be examined herein as they are drawn to the elected species, human.

Priority

3. The instant application is granted the benefit of priority for the U.S. non-Provisional Application No. 09/302,457 filed on April 29, 1999 as requested in the declaration and the first lines of the specification. The instant application is claimed as a continuation-in-part of 09/302,457, which does NOT disclose the human sequence as it is found in the instant specification (SEQ ID NOs:1 and 2). Therefore, the elected subject matter has priority back to only the filing date of the instant application that is November 26, 1999.

Information Disclosure Statement

4. No information disclosure statement has been filed with the instant application as of the date mailed of the instant Office action. Applicants are reminded that they have a duty to disclose all information, of which they are aware, relevant to the patentability of the pending claims (see 37 C.F.R. § 1.56 and M.P.E.P. § 2000). The Examiner notes that references are cited at the end of the specification; these references are not considered as an information disclosure.

Drawings

5. The drawings are considered informal for the reasons detailed in the attached copy of PTO Form 948. Appropriate correction is required prior to allowance.

Compliance with the Sequence Rules

6. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to **fully** comply with the requirements of 37 C.F.R. § 1.821

through 1.825; Applicants' attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990).

Applicants filed a paper copy and computer readable form copy of the sequence listing on August 16, 2001 (Paper No. 21) in response to a Notice to Comply (Paper No. 19); this sequence listing has been entered. This amendment did not contain a statement that the content of the paper and CRF copies include no new matter as required by 37 C.F.R. § 1.821 (e) or 1.821(f) or 1.821(g) or 1.821(b) or 1.825(d), and (4). Applicants must file such a statement.

Objections to the Specification

7. The specification is objected to improperly incorporating required materials by reference. On page 90, line 14, the description of the construction of AdRSVpHyde is incorporated from the parent application 09/302,457. Since the parent application is abandoned, the information is particularly difficult to obtain. The description of the construction of AdRSVpHyde must be added into the text of the instant application for completeness. Applicants must cite page and line number from the parent application to identify clear support as originally filed for any amendment.

8. The specification is objected to for containing confusing reference materials. Throughout the application, for example on page 25, line 25, bracketed references such as "[74]" are found but do not correlate to the reference citations at the end of the application. Amendment to these references must be added to include the proper citations. Also, "?" are found throughout the specification, for example on page 77, line 32. Their meaning is unclear and should be amended

into the specification. Applicants must cite page and line number from the instant application or any incorporated references to identify clear support as originally filed for any amendment.

9. In the specification, the Abstract is objected to for two reasons. The Abstract cannot be titled "Abstract of the Invention" since the abstract described the entire specification and the invention is particularly in the claims; the abstract must be titled ---Abstract--- or ---Abstract of the Disclosure---. The Abstract is also objected to for not completely describing the disclosed subject matter. It is noted that in many databases and in foreign countries, the Abstract is crucial in defining the disclosed subject matter, thus, its completeness is essential. The Abstract should not be a reiteration of the claims but should summarize the specification. The Examiner suggests the inclusion of the function of p-Hyde protein as well as the source species, human and rat, for completeness.

10. The title is objected to for not describing the claimed subject matter; the title included non-elected subject matter. The Examiner suggests deleting "and methods...in cancer" so that the title is properly descriptive of the claims.

Claim Objections

11. Claims 1, 7, 10-11, 16-27, 54-57 and 59-60 are objected to for containing non-elected subject matter. Only sequences and subject matter relating to the human sequence disclosed (SEQ ID NOs:1 and 2) will be examined. Non-elected subject matter must be canceled from Claims 1, 7, 10-11, 16-27, 54-57 and 59-60. Moreover, as noted above, Claim 58 is drawn solely

to the rat sequence as found in the virus sequences of SEQ ID NOs: 5 and 6. Therefore, Claim 58 is also withdrawn from consideration as a non-elected invention.

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 1, 7, 10-27, 54-57, and 59-60 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The instant claims refer to a claimed product that is an "isolated nucleic acid"; such products are small organic molecules, not genes. The instant claims should refer to ---nucleic acid sequences--- or ---polynucleotides--- for clarity.

13. Claims 1, 7, 10-27, 54-57, and 59-60 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In Claim 1, the term "analogs" when referring to a nucleic acid sequence is unclear. Must the activity be retained? Is so, what activity is that? Must the structure be retained? The metes and bound of the term "analog" are unclear.

14. Claims 12-15 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In Claim 12, line 2, the phrase "which encodes **the** human p-Hyde of

claim 1" (emphasis added) is unclear. Claim 1 refers to many mammalian p-Hyde genes. The above phrase should read ---which is a human p-Hyde nucleic acid sequence of Claim 1---.

15. Claim 16 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase "sequence complementary to" is unclear as to its metes and bounds since it further limits Claim 1. Claim 1 encompasses DNA, which is double stranded, already containing a "complementary" sequence to the gene that encodes the protein. Which sequence must it be complementary too?

16. Claim 19 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase "operatively, or an expression element linked to the nucleic acid" is wholly confusing. The position of the comma is confusing. Moreover, the need for two phrases describing the same thing is redundant.

17. Claims 21-24 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The abbreviations "BAC" and "P1" used in Claim 21 must defined upon their first appearance in the claims.

18. Claims 23-24 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The composition of the adenovirus vector, as found in Claim 23, is

wholly confusing. The clause should be rewritten. The Examiner suggests using language including where the deletion in the E1 and E3 region is replaced by the p-Hyde gene.

19. Claims 54-56 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term "similarity" is unclear as to its meaning. The metes and bounds are wholly confusing and not well-defined in the art.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

20. Claims 1, 7, 10-27, 54-56 and 59 are rejected under 35 U.S.C. § 112, first paragraph, written description, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The instant claims are drawn to nucleic acid sequences (or related products) wherein the product is defined *only* by function without any specific structural limitation. Claims 54-56 and 59 are included in the instant rejection based on the lack of clarity of the term "similarity" in reference to the structural limitation proposed in said claims; Claims 54-56 and 59 retain the functional limitation from Claim 1. Claims 57 and 60 are excluded from the instant rejection because they have a definite structure.

The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as be structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." University of California v. Eli Lilly and Co., 1997 U.S. App. LEXIS 18221, at *23, quoting Fiers v. Revel, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe a genus of genetic material, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these.

The instant specification discloses cDNA sequences from human (SEQ ID NO:1) and rat (SEQ ID NO:3) encoding a "p-Hyde" protein. This p-Hyde protein is disclosed as having the ability to induce cell-death-susceptibility in a cancer cell; this activity is tested using only the rat protein, which is 489 amino acids long; the deduced human protein is 186 amino acids long.

The specification adequately describes the two species of human and rat cDNA sequences encoding p-Hyde. The specification also adequately describes the genus of p-Hyde cDNAs whose structure and function are clearly related to the disclosed sequences, i.e., being at least 90% identical to SEQ ID NO:1 and encoding a protein having the ability to induce cell-death-susceptibility in a cancer cell. However, the structures of "analogs, fragments, variants, and mutants" and the structure of the "genomic" DNA related to the disclosed species cannot be

reasonably predicted by one of skill in the art using only the disclosed species as guides. No structural analysis of the p-Hyde cDNA is disclosed to indicate functional domains or the like. No information about introns can be predicted from the cDNA. Thus, when varying the disclosed sequence, one of skill in the art could not reasonably predict which portion of the sequences retain which homologies so that the claimed activity would be retained.

Claim Rejections - 35 U.S.C. § 101

35 U.S.C. § 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

21. Claims 1, 7, 10-27, 54-57, and 59-60 are rejected under 35 U.S.C. § 101 because the claimed invention lacks patentable utility. The instant claims are drawn to a nucleic acid sequence (p-Hyde gene) encoding a human p-Hyde protein. A p-Hyde protein from rat is characterized in the instant specification; the experiments presented for the rat protein indicate that rat p-Hyde has the ability to induce cell-death-susceptibility in a cancer cell. It can be reasonably assumed that other p-Hyde proteins from other mammals will possess the same, or closely related, activity. The utility of the claimed invention relies on the activity proposed for the rat protein.

The utility of the rat protein and gene cannot be translated into utility for the human protein and gene because is it unclear that the sequences are related. The instant specification discloses cDNA sequences from human (SEQ ID NO:1) and rat (SEQ ID NO:3) encoding a "p-Hyde" protein. These DNA sequences share a region of 84% identity (see attached alignment). The rat protein is 489 amino acids long from a cDNA open reading frame of 1467 base pairs.

The human protein is 186 amino acids long from a cDNA open reading frame of 637 base pairs (disclosed SEQ ID NO:1 also contains non-coding regions from 1-78 and from 638-733). It is not convincing that a rat protein of 489 amino acids would have a homolog in human of 186 amino acids, especially one so dissimilar in sequence. Moreover, no structural, domain analysis of the rat sequence has been offered to demonstrate a functional domain that is retained in the shorter human sequence. Thus, without convincing evidence that the disclosed human sequence actually encodes a p-Hyde homolog, the claimed nucleic acid sequences lack a patentable utility.

22. Claims 1, 7, 10-27, and 54-60 are also rejected under 35 U.S.C. 112, first paragraph, enablement. Specifically, since the claimed invention is not supported by either a credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

23. Claims 1, 7, 12, 13, 16, 17 are rejected under 35 U.S.C. § 102(b) as being anticipated by Hillier *et al.* (GenBank Accession Number R80991 (1995) yi94c03.r1 Soares placenta Nb2HP Homo sapiens cDNA clone IMAGE:146684 5', mRNA sequence). The instant claims are drawn to fragments of a human p-Hyde nucleic acid sequence.

Hillier *et al.* teach a human mRNA EST sequence that matches 155 nucleotides of Applicants' SEQ ID NO:1 (see attached alignment). Said EST will specifically hybridize with SEQ ID NO:1 and teaches the complementary or antisense sequences due to the inherent complimentarity of DNA molecules.

24. Claims 1, 7, 10-21, 25-27, 54-56 and 59 are rejected under 35 U.S.C. § 102(b) as being anticipated by Talerman *et al.* (WO 97/22695). The instant claims are drawn to human p-Hyde DNA sequences having some structural similarity to SEQ ID NO:1 (for Claims 54-56, the degree of relatedness is unclear). The claims are also drawn to nucleic acid sequences that are fluorescently labeled, vectors of said sequences including a BAC promoter, and mammalian host cell expression systems.

Talerman *et al.* teach a DNA sequence that is 72% similar and 39% identical to Applicants' SEQ ID NO:1 (see attached alignment). Talerman *et al.* also teach fluorescent labels on their DNA, hybridization techniques, and techniques using promoters, BAC vectors, and stably transfected murine host cells (see pages 15-16).

Noteworthy Prior Art

25. The following references are noted for the relatedness to the pending claims although said references are not available as prior art:

a) WO 00/11015 published March 2, 2000 by Valenzuela *et al.* See attached alignment.

b) GenBank Accession Number AY029585 (2001) Homo sapiens dudulin 2 mRNA, complete cds. 1845 bp mRNA. See attached alignment.

c) WO 01/18022 published March 15, 2001 by Ni *et al.* See attached alignment.

d) Rinaldy *et al.* Role of pHyde novel gene product as an intrinsic factor for apoptotic pathway in prostate cancer. Gan To Kagaku Ryoho 2000 May;27 Suppl 2:215-22.

e) Steiner *et al.* Growth inhibition of prostate cancer by an adenovirus expressing a novel tumor suppressor gene, pHyde. Cancer Res 2000 Aug 15;60(16):4419-25.

f) Zhang *et al.* Apoptosis induction in prostate cancer cells by a novel gene product, pHyde, involves caspase-3. Oncogene 2001 Sep 20;20(42):5982-90.

Examiner's Comment

26. For clarity of the record, the Examiner requests an explanation for the omission of Chiang Wang as an inventor of the claimed invention. Chiang Wang appears, with the other inventors, as an inventor in the WIPO document, WO 2000 071564 A2.

27. The Examiner suggests the inclusion of the 489 amino acid rat protein deduced from the 1467 base pair cDNA in the sequence listing. Often times, a disclosed protein can be overlooked because only its encoding DNA sequence is searchable (in a sequence listing). For completeness, the inclusion of the rat protein sequence is recommended. The rat full-length protein sequence would not be considered new matter if it is *exactly* encoded by the cDNA disclosed in SEQ ID NO:3. An alignment of the coding DNA and the added amino acid should be included to clearly show support and the lack of new matter.

PONNATHAPU ACHUTAMURTHY
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Conclusion

28. Claims 1, 7, 10-27, 54-57, and 59-60 are not allowed for the reasons identified in the numbered sections of this Office action. Applicants must respond to the objections/rejections in each of the numbered sections in this Office action to be fully responsive in prosecution.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kathleen M Kerr whose telephone number is (703) 305-1229. The examiner can normally be reached on Monday through Friday, from 8:30am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathupura Achutamurthy can be reached on (703) 308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-0294 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

PONNATHAPU ACHUTA MURTHY
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

KMK
March 22, 2002